RATIONALE FOR A HOSPITAL-BASED PNEUMOCOCCAL VACCINE TRIAL FOR HIV-SEROPOSITIVE SOUTH AFRICANS

In poor countries where affordable therapeutic options for human immunodeficiency virus (HIV) infection are extremely limited, the availability of cost-effective prophylactic measures to prevent opportunistic infection becomes vitally important. Bacterial pneumonia, especially due to the pneumococcus, is the most frequently encountered secondary infection complicating HIV disease in the teaching hospitals in Johannesburg and Soweto, South Africa.[1,2] Although its effectiveness in HIV-infected patients has not been demonstrated in prospective clinical trials, a case-control study has demonstrated benefit of pneumococcal vaccination in preventing invasive disease, and vaccine is currently recommended as for other high risk hosts.[3,4] However, the optimal location for administering pneumococcal vaccination to maximize usefulness is not clear. Hospital-based strategies have been recommended for several vaccines, including pneumococcal vaccine, to expand vaccine coverage. The authors sought to explore the rationale for a pre-discharge, hospital-based pneumococcal vaccination trial for patients with HIV infection in South Africa.

Culture logbooks of the Pneumococcal Research Unit Laboratory of the South African Institute for Medical Research (SAIMR) were retrospectively reviewed; they identified 104 patients with *Streptococcus pneumoniae* recovered from blood (n = 88 patients), cerebrospinal fluid (n = 9), or both (n = 7) during the 1997 calendar year. Of these, 94 patients were evaluable according to the available inpatient and HIV clinic medical records, and HIV enzyme-linked immunosorbent assay (ELISA) antibody and CD4+ cell count parameters. Dates of hospitalization for the 5 years prior to admission for pneumococcal infection as well as time of the first-positive HIV antibody result were retrieved from hospital medical records. No patients had received pneumococcal vaccination.

Seventy patients were 2 years of age or older; 24 patients were children less than 2 years of age. Where HIV antibody status was known, 92% were HIV-seropositive. Of the 53 HIV-seropositive persons 2 years of age or older, 20 (38%) had been hospitalized at least once during the previous 5 years (53 separate admissions), and a vast majority of patients were aware of their HIV status before or during the time of previous hospitalization. Human immunodeficiency virus antibody status was known by these patients before (62%), during (30%), or after (8%) hospitalization for pneumococcal disease; for children less than 2 years old, these figures were 29%, 71%, and 0%, respectively. Only 3 (6%) of 53 isolates from HIV-seropositive patients 2 years of age or older had CD4+ lymphocyte counts known before pneumococcal hospitalization, indicating poor HIV clinic enrollment in Johannesburg or Soweto. Subtyping of pneumococcal strains was not performed on all study isolates. If only serotypes (and not subtypes) were considered, up to 96% of invasive pneumococcal isolates from patients 2 years of age or older belonged to serotypes present in, or cross-reactive with the current 23-polyvalent polysaccharide pneumococcal vaccine; for children less than 2 years of age, 79% of isolates were contained in the 9-valent conjugate vaccine.

Observers have long identified missed opportunities, including hospitalization, where pneumococcal vaccine could be administered. In the United States, the Centers for Disease Control and Preventive (CDC) recommends administration of pneumococcal vaccine to inpatients as a strategy for improving vaccine coverage among adults.[5] Previous hospitalization has been shown to be a risk factor for subsequent serious pneumococcal infection, and modest levels of inpatient vaccination could substantially reduce hospital admissions.[6] Outpatient clinic-based pneumococcal immunization seems logical because it offers the advantage of identifying asymptomatic HIV-seropositive persons early in their infection. However, the authors' data indicate that although a majority of patients had been HIV antibody-tested prior to their hospitalization for pneumococcal disease, and thus knew their HIV status, a small percentage (6%) of these individuals were formally enrolled in any HIV clinic, as indicated by infrequent prior CD4+ cell count determinations (HIV clinics in Johannesburg and Soweto routinely perform baseline and follow-up CD4+ cell counts). Almost 40% of patients, however, had been hospitalized at least once, for any reason, during the preceding 4 years, thereby representing instances where pneumococcal vaccine could have been administered, to prevent future infection. In-hospital, pre-discharge HIV testing and pneumococcal vaccination, perhaps combined with outpatient HIV site testing vaccination could increase pneumococcal vaccine coverage among HIV-infected patients in South Africa. Vaccination of hospitalized patients with first-episode pneumococcal disease might also have an important role in reducing the high rates of second pneumococcal infections.[7] In light of concern about the efficacy and safety of pneumococcal vaccine in HIV-infected Africans,[8] its use should be evaluated in further clinical trials.

REFERENCES

1. Walkden D, Patel J, Snipeliski M, Heney C. HIV statistics at Baragwanath Hospital, March 1988 to June 1989. Presented

at the 32nd South African Congress for Pathology and Microbiology, Pretoria, May 18-20, 1992.
2. Jentsch U, Spencer DA. Causes of mortality in HIV-seropositive patients seen at the Johannesburg Hospital, South Africa, 1991-1995. Presented at the 36th South African Congress for Pathology and Microbiology, Pretoria, June 1996.
3. Gebo KA, Moore RD, Kenily JC, Chaisson RE. Risk factors for pneumococcal disease in human immunodeficiency virus-infected patients. J Infect Dis 1996; 173:857-862.
4. Fedson DS, Musher DM. Pneumococcal vaccine. In: Plotkin SA, Mortimer EA Jr, eds. Vaccines. 2nd Ed. Philadelphia, PA: WA Saunders, 1994;517-564.
5. Centers for Disease Control and Prevention. Pneumococcal and influenza vaccination levels among adults aged over 65 years: United States, 1995. MMWR Morb Mortal Wkly Rep 1997; 46:913-919.
6. Fedson DS. Improving the use of pneumococcal vaccine through a strategy of hospital-based immunization: a review of the rationale and implications. J Am Geriatr Soc 1986; 33:142-150.
7. Jordens JZ, Paul J, Bates J, Beaumont C, Kimari J, Gilks G. Characterization of *Streptococcus pneumoniae* from HIV-seropositive patients with acute and recurrent pneumonia. J Infect Dis 1995; 172:983-987.
8. Gilks GF, French N, Nakiyingi J, et al. Lack of efficacy of 23-valent pneumococcal polysaccharide vaccine in HIV-infected Ugandan adults. Presented at the Pneumococcal Vaccine for the World Conference. Bethesda, MD, September 1998.

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FOOD IRRADIATION AND VITAMIN LOSS

I am writing in response to Dr. Donald B. Louria's "Counterpoint on Food Irradiation," which I think contains some misleading statements about food irradiation in the United States as well as about the effects of irradiation on the nutritional value of foods.

Dr. Louria expresses great concern about losses of vitamins and, possibly, other nutrients as a result of food irradiation. No reputable nutritionist would deny that irradiation can lower the vitamin content of foods. Thiamin and vitamin C likely are the most vulnerable, but the losses of thiamin as a result of irradiation of beef, for example, are less than that which occurs with canning or other thermal processing. And vitamin C losses when fruits and vegetables are irradiated are "small relative to the natural variance in vitamin C content."[1] Pasteurization of milk results in losses of vitamin B_{12} (10%), thiamin (10%), vitamin C (10-25%), and folic acid (10%); but the national acceptance of milk pasteurization has not resulted in widespread deficiencies of these nutrients (none of which are added back to milk).[2]

Further, Dr. Louria's letter seems to imply that all foods would be irradiated if the process were widely accepted, and that consumers would not be informed that their foods are irradiated. First, it is unclear that producers have any intention of irradiating all foods. Second, it is already required that any irradiated foods on sale in retail stores be identified by the green radura symbol—a flower in a broken circle. So consumers not only will be informed of which foods are irradiated but also will have a choice as to whether to buy them.

Dr. Louria expresses concerns about the approximately 16 million older Americans who he says have low blood levels of at least one vitamin. Is he not concerned about the older Americans who are particularly susceptible to the adverse effects of food poisoning, or about people taking immunosuppressant medications who also are more susceptible?

Currently, most Americans are in very little danger of nutrient deficiency. Citing small nutrient losses as a consequence of irradiation, or any food processing technique, to inveigh against that process denies a huge body of scientific literature on the wholesomeness and enhanced safety of foods so treated.

References

1. Williams AW, Erdman JW Jr. Food processing: nutrition, safety, and quality balances. In: Shils ME, Olson JA, Shike M, Ross AC, eds. Modern nutrition in health and disease. 9th Ed. Baltimore: Williams & Wilkins, 1999.
2. Swaisgood HE. Characteristics of edible fluids of animal origin: milk. In: Fennema OR, ed. Food chemistry. 2nd Ed. New York: Marcel Dekker, Inc., 1985.

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ARE THERE VALID CONCERNS ABOUT FOOD IRRADIATION?

Dr. Louria's "Counterpoint on Food Irradiation," presents several questions of the proponents and processors of irradiated foods. The following is a response to those points.

Dr. Louria's first point is that he does not believe that Dr. Steele used the current analysis of food-related illnesses and cites the data of Mead et al.[1] However, upon closer inspection, I note that Dr. Steele mentions "An estimated 76,000,000 cases of foodborne infection...approximately 6000 deaths." Mead estimates 76 million